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EXAMINER	
HANLEY, SUSAN MARIE	
ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/777,461	HAWKINS ET AL.	
	Examiner	Art Unit	
	Susan Hanley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-67 and 69* is/are pending in the application.

4a) Of the above claim(s) *2,4,5,9-11,16-21,27-32,37,45,46,48,53 and 57-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,6-8,12-15,22-24,33-36,38-44,47,49-52,54-56,65-67 and 69* is/are rejected.

7)☒ Claim(s) *25,40 and 41* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 February 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment and reply filed 7/24/07 are acknowledged.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-42, 56 and 69; and the following specie election:

A. Quenching agent for the first or second enzyme-mediated reaction: a sequestering agent that is a nonionic detergent;

B. First enzyme-mediated luminescence reaction: Renilla reniformis luciferase-mediated;

C. Second enzyme-mediated luminescence reaction: Photinus pyralis luciferase-mediated;

in the reply filed on 1/31/07 is again acknowledged. Applicants' traversal was found persuasive, in part. Groups I and II (method and kit) were rejoined insofar as they read on the elected species.

Claims 2, 4, 5, 9-11, 16-21, 27-32, 37, 45, 46, 48, 53 and 57-64 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected invention and species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/31/07.

Claims 1, 3, 6-8, 12-15, 22-24, 33-36, 38-44, 47, 49-52, 54-56, 65-67 and 69 remain under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawal of Rejections

The objections and rejection not explicitly restated below are withdrawn due to Applicant's response in the amendment filed 7/24/07.

Drawings

Applicant traverses the objection to Figure 5 as being prior art because there is no support for the objection.

Figure 5 is a recitation of the properties of detergents. The figure includes references for the sources of the properties. Hence, the recitation of detergent properties from the prior art should have a legend stating such. See MPEP § 608.02(g). Corrected drawings in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance. Furthermore, it is noted that there are several non-numbered pages that are part of Figure 5. All drawing figures should be numbered. Additionally, there should be one Figure per page. Figures with multiple pages can always be numbered as 5A, 5B, etc.

Response to Arguments

Claim Rejections - 35 USC § 102

Claims 1, 3, 6-8, 12, 13, 22-24, 32-36, 38-42, 44, 49 and 54 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Sherf et al. (US 5,744,320; cited in the IDS filed 9/17/04).

Applicant summarizes that Sherf discloses a dual-enzyme reporter assay that employs Renilla luciferase and fire-fly luciferase. Applicant states that Sherf discloses reagents useful to quench one reaction without quenching the subsequent reaction. Applicant asserts that Sherf does

not disclose or suggest (1) a method or kit for a selective quench agent for a non-beetle luciferase reaction by at lest 35-fold; or (2) a selective quench reagent for an anthozoan luciferase; (3) a kit having at least one selective quench reagent that is a nonionic detergent that is not Triton X-100 or Tween 20; (4) a substrate analog inhibitor for an anthozoan luciferase; (5) a colored compound or a combination thereof.

Responding to argument (1), *Renilla reniformis* is a sea pansy from class *Anthozoa (see printout out from the "infoplease" website)* and *Photinus pyralis* is a firefly. Neither of these organisms that supply luciferase are beetles and they meet the "non-beetle" limitation. Responding to argument and Sherf teaches that the luciferase-mediated reaction is preferably quenched by reducing photon emissions from the first luciferase-mediated luminescence reaction by a factor of at least 1,000-fold (col. 9, lines 33-38). 1,000-fold is greater than 35-fold. Hence the limitation is met; (2), *Renilla reniformis* is a sea pansy from class *Anthozoan.* In Table 3, Sherf discloses that *Renilla* luciferase luminescence can be quenched by Tween®20 or Triton®X-100. The disclosure of Tween®20 and Triton®X-100 meets the limitations of a selective sequestering agent that is a nonionic detergent, as in instant claims 6-8. Responding to arguments (3-5), claims 44, 49 and 54 (as it depends from claim 49) do not recite these limitations. The claims that have been amended to recite these limitations are no longer rejected by Sherf alone.

New Grounds of Objection and Rejection

Claim Objections

Claim 40 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the

claim(s) in independent form. The limitation of quenching the first enzyme-mediated luminescence reaction by at least 35-fold is recited in claim 1.

Claims 25, 40 and 41 are objected to because they depend from claim 2 which has been withdrawn from examination..

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention..

Claims 14, 15, 43, 47,50-52, 55, 56, 65-67 and 69 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for determining luminescence energy produced by a first and second luciferase-mediated luminescence reaction wherein at least one of said luciferases is anthozoan and the luminescence generated by the anthozoan luciferase is selectively quenched by coelenterazine hh methyl ester; colored compounds that absorb red, yellow, green and blue wavelengths of light as disclosed on page 31, lines 11-19 of the specification; and nonionic detergents prior to initiating the second luminescent reaction; and determining the luminescence produced by the second reaction; and a kit thereof, does not reasonably provide enablement for said method or kit wherein the first enzyme mediated reaction is provided by any non-beetle luciferase or the selective quenching of the first enzyme mediated reaction is by any possible substrate analog inhibitor for an anthozoan luciferase or a protected coelenterazine or any possible colored compound. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The indicated claims are broadly drawn to a dual reporter assay based on at least two enzyme-mediated luminescent reactions and the selective quenching of the first reaction by a nonionic detergent, a colored compound or a substrate analog inhibitor for an anthozoan luciferase or a protected coelenterazine. The specification provides enabling disclosure for a first enzyme-mediated bioluminescent that is an anthozoan luciferase and selective quenching agents for said anthozoan luciferase that are nonionic detergents but does not fully enable the scope of any possible enzyme-mediated luminescent reaction and the indicated broad classes of quenching agents.

The limited showing of the combination one type of molecule that generates a bioluminescent reaction, e.g., an anthozoan luciferase, that is selectively quenched by coelenterazine hh methyl ester, and colored compounds that absorb red, yellow, green and blue wavelengths of light as disclosed on page 31, lines 11-19 prior to initiating the second luminescent reaction is not sufficient to enable a claim drawn to the quenching of any possible enzyme-mediated reaction by the indicated broad classes of quenching agent because the art of Enzymology is too unpredictable. It is well known in the art that enzymes with the same catalytic activity could come from diverse origins, be substantially different in size and even have different catalytic mechanisms. The use of enzymes requires knowledge of a process for preparing them, knowledge of working conditions under which the enzyme retains activity and provision of any co-factors required under which the enzymatic reaction in question. The specification does not disclose if the reported selective quenching of anthozoan luciferase by coelenterazine hh methyl ester, colored compounds

that absorb red, yellow, green and blue colored wavelengths of light as disclosed on page 31, lines 11-19 prior to initiating the second luminescent reaction is a reliable, repeatable method that can be utilized for the inhibition or quenching of any possible enzyme-mediated reaction by the indicated broad classes of quenching agent.

In fact, the prior art teaches away from this concept. Ward (cited in the IDS filed 9/17/04) disclose that the substrates, generally known as luciferins, of light emitting systems of luminescent organisms greatly differ in structure. For example, the compounds shown on page 323 display a wide variation of structures of the various luciferin substrates for firefly, the freshwater limpet *Latia*, luminous bacteria, the crustacean *Cypridina*, luminescent jellyfish and so on. The great differences in molecular structure of the luciferin substrates makes it unlikely that the luciferase enzyme of each organism is the same enzyme or an isozyme. Hence, it follows that enzymes of luminescent organisms which catalyze a luciferin reaction would be tailored for the particular substrate structure of said organism. The same concept applies to inhibitors. The complex structure of enzymes and their active sites drives the structures of compounds that can inhibit said enzymes. Again, the great differences in molecular structure of the luciferin enzymes makes it unlikely that the luciferase enzyme of each organism is will be inhibited by the same inhibitors and the skilled artisan would be obliged to a trial and error process to determine the inhibition or quenching of any possible enzyme-mediated reaction by the indicated broad classes of quenching agent. Such a trial and error process clearly amounts to undue experimentation.

The specification is enabled on for the substrate analog inhibitor, coelenterazine hh methyl ester. The specification presents a generic structure based on coelenterazine (p. 19) that allegedly directs the skilled artisan to other substrate analog inhibitors. However, this structure also reads

on many coelenterazine substrates for anthozoan luciferases. The specification provides no guidance that would *a priori* direct the skilled artisan to intelligently select compounds that will be inhibitors and not substrates for the intended luciferase with a reasonable degree of predictability. The design of substrate-based inhibitors requires detailed knowledge about the active site of an enzyme. Without some disclosure regarding the active site, the skilled artisan could not predict which compounds based on the disclosed generic structure would be inhibitors and not substrates for the anthozoan luciferase. Hence, the skilled artisan would have to resort to trial and error testing of compounds to find inhibitors and not substrates. Such a trial and error process clearly amounts to undue experimentation.

Likewise, the specification is enabled on for colored compounds that absorb red, yellow, green and blue wavelengths of light as disclosed on page 31, lines 11-19. The specification fails to provide a discussion on the interaction between different wavelengths of light, substrate and luciferase such that the skilled artisan could reliably predict which types of wavelengths will be generated by the bioluminescent reaction and the corresponding colored compounds that will quench said light with a reasonable degree of predictability. Without some direction regarding what wavelength of light will be generated by the reaction of a particular luciferase and substrate, the skilled artisan could not predict which colored compounds could absorb the generated wavelength of light to selectively quench the reaction. Hence, the skilled artisan would have to resort to trial and error testing to determine what combination of luciferase, substrate and generated light could be absorbed by a particular colored compound. Such a trial and error process clearly amounts to undue experimentation.

Undue experimentation would be required to practice the invention as claimed due to the quantity of experimentation necessary; limited amount of guidance and limited number of working examples in the specification; nature of the invention; state of the prior art; relative skill level of those in the art; predictability or unpredictability in the art; and breadth of the claims. *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14, 15, 43, 50-52, 34-36, 55, 56, 65-67 and 69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "functional equivalent thereof" is indefinite because it is not clear what functional aspect of the parent luciferase is being described.

Claims 14, 43, 47, 50, 52,55, 56, 65 and 69 contain the trademark/trade names Triton® and Tween®. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is

used to identify/describe types of nonionic detergents and, accordingly, the identification/description is indefinite.

Claims 15, 35, 36, 51, 66 and 67 are dependent claims that do not overcome the deficiencies of the independent claim that they are dependent therefrom.

Claim Rejections - 35 USC § 103

Claims 14, 15, 43, 47,50-52, 55, 56, 65-67 and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sherf et al. (US 5,744,320; cited in the IDS filed 9/17/04) in view of The Sigma Catalog (1998).

The disclosure by Sherf is discussed *supra*.

Sherf does not disclose the method or kit wherein the first enzyme-mediated reaction is quenched with a nonionic detergent that is not Tween®20 or Triton®X-100.

The Sigma Catalog discloses a list of 27 nonionic detergents for biollogical applications (p. 1879).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to test any of the 27 detergents disclosed by Sigma in the method or kit wherein the first enzyme-mediated reaction is quenched with a nonionic detergent as taught by Sherf. The ordinary artisan would have been motivated to do so because Sigma sells additional nonionic detergents that may have an equal or better effect than Tween®20 or Triton®X-100. The ordinary artisan would have realized that nonionic detergents have the same mechanism of sequestration and the testing of a limited number of nonionic detergents (that are easily obtained) would serve to optimize the selective quenching step of the assay.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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